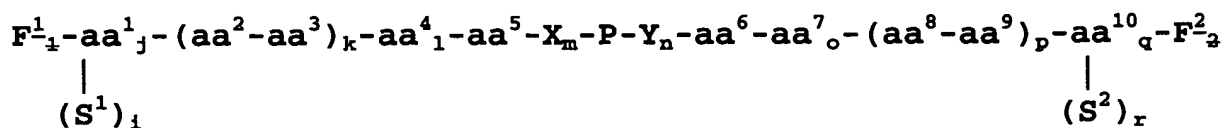


AMENDMENTS TO THE CLAIMS

Claim 1 (Currently amended): A fluorogenic composition for the detection of the activity of a protease, said composition having the formula:



wherein, P is a peptide ~~selected from the group~~ consisting of the amino acid sequence ~~IETDSGV (SEQ ID NO:208), SEVNLD AEF (SEQ ID NO:209), and YVHDAPV (SEQ ID NO:210);~~

F<sup>1</sup> and F<sup>2</sup> are fluorophores and F<sup>1</sup> is attached to the amino terminal amino acid and F<sup>2</sup> is attached to the carboxyl terminal amino acid;

S<sup>1</sup> and S<sup>2</sup>, when present, are peptide spacers ranging in length from 1 to about 50 amino acids and S<sup>1</sup>, when present, is attached to the amino terminal amino acid and S<sup>2</sup>, when present, is attached to the carboxyl terminal amino acid;

i, j, k, l, m, n, o, p, q, and r are independently 0 or 1;

aa<sup>1</sup> and aa<sup>10</sup> are independently selected from the group consisting of lysine, ornithine and cysteine;

aa<sup>2</sup>, aa<sup>3</sup>, aa<sup>8</sup>, and aa<sup>9</sup> ~~and aa<sup>9</sup>~~ aa<sup>2</sup>-aa<sup>3</sup>-, and -aa<sup>8</sup>-aa<sup>9</sup>- are independently selected from the group consisting of an amino acid or a dipeptide where said amino acid or dipeptide consist of amino acids selected from the group consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, homoserine, Thr, and Tyr;

aa<sup>5</sup>, aa<sup>4</sup>, aa<sup>6</sup>, and aa<sup>7</sup> are independently selected from the group consisting of proline, 3,4-dehydropoline, hydroxyproline, alpha aminoisobutyric acid and N-methyl alanine;

X is selected from the group consisting of Gly, βAla, γAbu, Gly-Gly, Ahx, βAla- Gly, βAla-βAla, γAbu-Gly, βAla-γAbu, Gly-Gly-Gly, γAbu-γAbu, Ahx-Gly, βAla-Gly-Gly, Ahx-βAla, βAla-βAla-Gly, Gly-Gly-Gly-Gly, Ahx-γAbu, βAla-βAla-βAla, γAbu-βAla-Gly, γAbu-γAbu-Gly, Ahx-Ahx, γAbu-γAbu-βAla, and Ahx-Ahx-Gly;

Y is selected from the group consisting of Gly, βAla, γAbu, Gly-Gly, Ahx, Gly-βAla, βAla-βAla, Gly-γAbu, γAbu-βAla, Gly-Gly-Gly, γAbu-γAbu, Gly-Ahx, Gly-Gly-βAla, βAla-

Ahx, Gly- $\beta$ Ala- $\beta$ Ala, Gly-Gly-Gly-Gly (SEQ ID NO:211),  $\gamma$ Abu-Ahx,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala, Gly- $\beta$ Ala- $\gamma$ Abu, Gly- $\gamma$ Abu- $\gamma$ Abu, Ahx-Ahx,  $\beta$ Ala- $\gamma$ Abu- $\gamma$ Abu, and Gly-Ahx-Ahx; and

when i is 1, S<sup>1</sup> is joined to aa<sup>1</sup> by a peptide bond through a terminal alpha amino group of aa<sup>1</sup>; and when r is 1, S<sup>2</sup> is joined to aa<sup>10</sup> by a peptide bond through a terminal alpha carboxyl group of aa<sup>10</sup>.

Claim 2 (Original): The composition of claim 1, wherein the carboxyl terminal amino acid in which the carboxylic acid group is replaced with an amide.

Claim 3 (Currently amended): The composition of claim 1, wherein:

r is zero; and

aa<sup>10</sup> has a C-terminal amide group or free carboxylic acid group.

Claim 4 (Currently amended): The composition of claim 1, comprising an amino acid sequence selected from the group consisting of KDPJGYVHDAPVGJPKG Y (SEQ ID NO:171), ~~KDPJGYVHDAPVPKG Y~~, and KDPYVHDAPVGJPKG Y (SEQ ID NO:172).

Claim 5 (Original): The composition of claim 4, wherein said composition has a terminal blocking group.

Claim 6 (Currently amended): The composition of claim 4, wherein said composition has a terminal 9-fluoreneacetyl (Fa) group.

Claim 7 (Currently amended): The composition of claim 4, wherein said composition has a terminal 9-fluorenylmethoxycarbonyl (Fmoc) group.

Claim 8 (Canceled).

Claim 9 (Original): The composition of claim 1, wherein F<sup>1</sup> and F<sup>2</sup> are the same fluorophore.

Claim 10 (Original): The composition of claim 9, wherein said F<sup>1</sup> and F<sup>2</sup> have an excitation wavelength between about 315 nm and about 800 nm.

Claim 11 (Original): The composition of claim 1, wherein the F<sup>1</sup> molecule is attached through either an  $\alpha$ -amino group of the aa<sup>1</sup> amino acid or through a side chain amino group of the aa<sup>1</sup> amino acid, or through a sulfhydryl group of a side chain of the aa<sup>1</sup> amino acid.

Claim 12 (Original): The composition of claim 1, wherein the F<sup>2</sup> molecule is attached either through a side chain amino group of the aa<sup>10</sup> amino acid, through a carboxyl group of the aa<sup>10</sup> amino acid, or through a sulfhydryl group of a side chain of the aa<sup>10</sup> amino acid.

Claim 13 (Currently amended): The composition of claim 1, wherein said fluorophore is selected from the group consisting of rhodamine X, ~~9-(2,5 (or 2,6)-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthyliumhalide~~ 9-(2,5-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthyliumhalide or other anion (TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthyliumhalide or other anion (TMR), 9-(2,5)-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium halide or other anion (Rh6G), 9-(2,6)-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium halide or other anion, ~~9-(2,5 (or 2,6)-dicarboxyphenyl)-3,6-bisamino-xanthylium halide~~ or other anion (Rh110), 9-(2,5-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), 9-(2,6-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), ~~9-(2,5 (or 2,6)-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide~~ or other anion (Blue Rh), 9-(2,5-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), 9-(2,6-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), carboxytetramethylrhodamine, carboxyrhodamine-X, diethylaminocoumarin, 9-(2,5-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (5-TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (6-TMR), 9-(2-carboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium, 9-(2-carboxyphenyl)-3,6-bis(dimethylamino)xanthylium, and 9-(2-carboxyphenyl)-xanthylium.

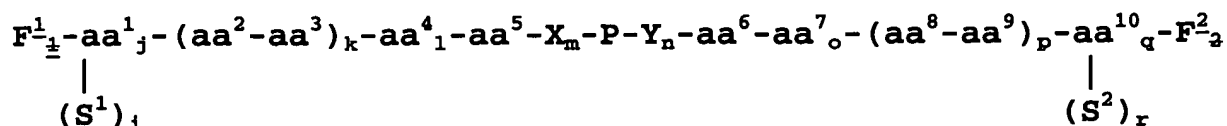
Claim 14 (Original): The composition of claim 1, wherein said fluorophore comprises a carbocyanine dye.

Claim 15 (Original): The composition of claim 1, wherein said composition bears a hydrophobic group.

Claim 17 (Currently amended): The composition of claim 16, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group, 1-fluorene-carboxylic group, 9-fluorene-carboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthyl (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), ~~4,4-dimethoxybenzhydryl (Mbh)~~, Tosyl (Tos), 4,4-dimethoxybenzhydryl (Mbh), 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimethyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO), t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

Claim 19 (Original): The composition of claim 17, wherein said hydrophobic group is Fa.

Claim 21 (Currently amended): A fluorogenic composition for the detection of the activity of a protease, said composition having the formula:



$F^1$  and  $F^2$  are fluorophores and  $F^1$  is attached to the amino terminal amino acid and  $F^2$  is attached to the carboxyl terminal amino acid;

$S^1$  and  $S^2$ , when present, are peptide spacers ranging in length from 1 to about 50 amino acids and  $S^1$ , when present, is attached to the amino terminal amino acid and  $S^2$ , when present, is attached to the carboxyl terminal amino acid;

i, j, k, l, m, n, o, p, q, and r are independently 0 or 1;

$aa^1$  and  $aa^{10}$  are independently selected from the group consisting of lysine, ornithine and cysteine;

$aa^2$ ,  $aa^3$ ,  $aa^8$ , and  $aa^9$  ~~and  $aa^9$~~   $-aa^2-aa^3-$ , and  $-aa^8-aa^9-$  are independently selected from the group consisting of an amino acid or a dipeptide where said amino acid or dipeptide consist of amino acids selected from the group consisting of Asp, Glu, Lys, Ornithine, Arg, Citulline, homocitrulline, Ser, homoserine, Thr, and Tyr;

$aa^5$ ,  $aa^4$ ,  $aa^6$ , and  $aa^7$  are independently selected from the group consisting of proline, 3,4-dehydropyrrolidine, hydroxyproline, alpha aminoisobutyric acid and N-methyl alanine;

X is selected from the group consisting of Gly,  $\beta$ Ala,  $\gamma$ Abu, Gly-Gly, Ahx,  $\beta$ Ala-Gly,  $\beta$ Ala- $\beta$ Ala,  $\gamma$ Abu-Gly,  $\beta$ Ala- $\gamma$ Abu, Gly-Gly-Gly,  $\gamma$ Abu- $\gamma$ Abu, Ahx-Gly,  $\beta$ Ala-Gly-Gly, Ahx- $\beta$ Ala,  $\beta$ Ala- $\beta$ Ala-Gly, Gly-Gly-Gly-Gly, Ahx- $\gamma$ Abu,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala,  $\gamma$ Abu- $\beta$ Ala-Gly,  $\gamma$ Abu- $\gamma$ Abu-Gly, Ahx-Ahx,  $\gamma$ Abu- $\gamma$ Abu- $\beta$ Ala, and Ahx-Ahx-Gly;

Y is selected from the group consisting of Gly,  $\beta$ Ala,  $\gamma$ Abu, Gly-Gly, Ahx, Gly- $\beta$ Ala,  $\beta$ Ala- $\beta$ Ala, Gly- $\gamma$ Abu,  $\gamma$ Abu- $\beta$ Ala, Gly-Gly-Gly,  $\gamma$ Abu- $\gamma$ Abu, Gly-Ahx, Gly-Gly- $\beta$ Ala,  $\beta$ Ala-Ahx, Gly- $\beta$ Ala- $\beta$ Ala, Gly-Gly-Gly-Gly (SEQ ID NO:214),  $\gamma$ Abu-Ahx,  $\beta$ Ala- $\beta$ Ala- $\beta$ Ala, Gly- $\beta$ Ala- $\gamma$ Abu, Gly- $\gamma$ Abu- $\gamma$ Abu, Ahx-Ahx,  $\beta$ Ala- $\gamma$ Abu- $\gamma$ Abu, and Gly-Ahx-Ahx; and

when i is 1,  $S^1$  is joined to  $aa^1$  by a peptide bond through a terminal alpha amino group of  $aa^1$ ; and when r is 1,  $S^2$  is joined to  $aa^{10}$  by a peptide bond through a terminal alpha carboxyl group of  $aa^{10}$ .

~~terminal alpha carboxyl group of  $aa^{10}$ ;~~

Claim 22 (Original): The composition of claim 21, wherein the carboxyl terminal amino acid in which the carboxylic acid group is replaced with an amide.

Claim 23 (Original): The composition of claim 21, wherein:

r is zero; and

aa<sup>10</sup> has a C-terminal amide group or free carboxylic acid group.

Claim 24 (Currently amended): The composition of claim 21, comprising an amino acid sequence selected from the group consisting of KDBYVHDAPVPGGY (SEQ ID NO: ~~245~~218), KDBGYVHDAPVGPGGY (SEQ ID NO: ~~246~~219), KDBJGYVHDAPVGJPGGY (SEQ ID NO: ~~247~~220), and KDBJG(dY)VHDAPVGJPGGY (SEQ ID NO: ~~248~~221).

Claim 25 (Original): The composition of claim 24, wherein said composition has a terminal blocking group.

Claim 26 (Original): The composition of claim 24, wherein said composition has a terminal Fa group.

Claim 27 (Original): The composition of claim 24, wherein said composition has a terminal Fmoc group.

Claim 28 (Original): The composition of claim 21, wherein F<sup>1</sup> and F<sup>2</sup> are the same fluorophore.

Claim 29 (Original): The composition of claim 28, wherein F<sup>1</sup> and F<sup>2</sup> have an excitation wavelength between about 315 nm and about 800 nm.

Claim 30 (Original): The composition of claim 21, wherein the F<sup>1</sup> molecule is attached through either an  $\alpha$ -amino group of the aa<sup>1</sup> amino acid or through a side chain amino group of the aa<sup>1</sup> amino acid, or through a sulfhydryl group of a side chain of the aa<sup>1</sup> amino acid.

Claim 31 (Original): The composition of claim 21, wherein the F<sup>2</sup> molecule is attached either through a side chain amino group of the aa<sup>10</sup> amino acid, through a carboxyl group of the aa<sup>10</sup> amino acid, or through a sulfhydryl group of a side chain of the aa<sup>10</sup> amino acid.

Claim 32 (Currently amended): The composition of claim 21, wherein said fluorophore is selected from the group consisting of rhodamine X, ~~9-(2,5-(or 2,6)-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthylumhalide~~ 9-(2,5-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthylumhalide or other anion (TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis(dimethylamino)xanthylumhalide or other anion (TMR), 9-(2,5 )-dicarboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylum halide or other anion (Rh6G), 9-(2,6 )-dicarboxyphenyl)-2,7-dimethyl-

3,6-bis(ethylamino)xanthylium halide or other anion, ~~9-(2,5 (or 2,6)-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), 9-(2,5-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), 9-(2,6-dicarboxyphenyl)-3,6-bisamino-xanthylium halide or other anion (Rh110), 9-(2,5 (or 2,6)-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), 9-(2,5-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh), 9-(2,6-dicarboxyphenyl)-3-amino-6-hydroxy-xanthylium halide or other anion (Blue Rh),~~  
carboxytetramethylrhodamine, carboxyrhodamine-X, diethylaminocoumarin, 9-(2,5-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (5-TMR), 9-(2,6-dicarboxyphenyl)-3,6-bis-(dimethylamino)xanthylium chloride (6-TMR), 9-(2-carboxyphenyl)-2,7-dimethyl-3,6-bis(ethylamino)xanthylium, 9-(2-carboxyphenyl)-3,6-bis(dimethylamino)xanthylium, and 9-(2-carboxyphenyl)-xanthylium.

Claim 33 (Original): The composition of claim 21, wherein said fluorophore comprises a carbocyanine dye.

Claim 34 (Original): The composition of claim 21, wherein said composition bears a hydrophobic group.

Claim 35 (Currently amended): The composition of claim 34, wherein said hydrophobic group is selected from the group consisting of: Fmoc, 9-fluoreneacetyl group, 1-fluorene-carboxylic group, 9-fluorene-carboxylic group, and 9-fluorenone-1-carboxylic group, benzyloxycarbonyl, Xanthy (Xan), Trityl (Trt), 4-methyltrityl (Mtt), 4-methoxytrityl (Mmt), 4-methoxy-2,3,6-trimethyl-benzenesulphonyl (Mtr), Mesitylene-2-sulphonyl (Mts), ~~4,4-dimethoxybenzhydryl (Mbh)~~, Tosyl (Tos), ~~4,4-dimethoxybenzhydryl (Mbh)~~, 2,2,5,7,8-pentamethyl chroman-6-sulphonyl (Pmc), 4-methylbenzyl (MeBzl), 4-methoxybenzyl (MeOBzl), Benzyloxy (BzlO), Benzyl (Bzl), Benzoyl (Bz), 3-nitro-2-pyridinesulphenyl (Npys), 1-(4,4-dimethyl-2,6-diaxocyclohexylidene)ethyl (Dde), 2,6-dichlorobenzyl (2,6-DiCl-Bzl), 2-chlorobenzyloxycarbonyl (2-Cl-Z), 2-bromobenzyloxycarbonyl (2-Br-Z), Benzyloxymethyl (Bom), t-butoxycarbonyl (Boc), cyclohexyloxy (cHxO), t-butoxymethyl (Bum), t-butoxy (tBuO), t-Butyl (tBu), Acetyl (Ac), and Trifluoroacetyl (TFA).

Claim 36 (Original): The composition of claim 21, wherein said hydrophobic group is Fmoc.

Claim 37 (Original): The composition of claim 21, wherein said hydrophobic group is Fa.

Claim 38 (Original): The composition of claim 21, wherein said hydrophobic group is attached to the amino terminus of the molecule.

Claims 39-61 (Canceled).